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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/190,246 | 11/13/1998 | MARK PARRINGTON | 1038-865MIS | 6436 |

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| ART UNIT | PAPER NUMBER |
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| 1632 | |

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13

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/190,246 | Applicant(s) PARRINGTON ET AL. | |
|---|---|---|---|
| | Examiner Michael Wilson | Art Unit 1632 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *30 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,6,8-10,14-19 and 36-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6,8-10,14-19 and 36-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *detailed action* .

## DETAILED ACTION

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1632.

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5-20-02, paper number 22, has been entered.

Applicant's amendment filed 11-14-01, paper number 19, has been entered. Claims 7 and 11-13 have been canceled. Claims 1, 6, 8-10, 14-19 and 36-38 are pending and under consideration in the instant application.

The references in the PTO-1449 filed 5-30-02 are duplicates of the references in the PTO-1449 filed 11-10-99, paper number 7, which have already been considered. It is noted that the references therein are not in the correct format. Foreign patent document citations should include the inventor name. "Other documents" citations should include the title. The author of "Other documents" citations can be compressed to the last name of the first author and include "et al." if there is more than one author.

Applicants arguments filed 11-14-01, paper number 19, have been fully considered but they are not persuasive. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Specification***

1. The attempt to incorporate subject matter into this application by reference to US application 08/923558 is improper because the method of immunizing the mice is considered essential to practice the invention. The relevant information regarding the method of immunizing the control group should be included in the instant specification. The results obtained in applications 08/923,558, 08/476,397 and 08/896,500 are not included in the instant specification (page 26, line 22). The comparison of the results obtained in example 3 of the instant invention to the results obtained in another application is essential subject matter; therefore, such results should be included in the specification.

2. The status of the US Patent applications on pg 5, line 11, pg 6, line 30, pg 7, line 6, pg 7, line 12, pg 7, line 6, pg 9, line 13, pg 9, line 29, pg 15, line 14, pg 15, line 15, pg 15, line 18, pg 15, line 19, pg 23, line 25, pg 24, line 23, pg 25, line 18, pg 26, line 24, pg 26, line 25, must be updated. Contrary to applicants statement, 09/190245 has been abandoned.

3. The addition of the ATCC designation 203461 deposited 11-18-98 on page 22, line 10 remains new matter. The deposit information provided indicates the deposit was received 11-12-98. Please amend the specification accordingly.

Applicants have not provided any evidence that the inventors of the instant application deposited 203461 or that the deposit will be maintained according to the Budapest treaty.

If the deposit was made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicants, assignees or a statement by an attorney of record over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required.

Applicants have not provided such an affidavit or declaration. Applicants argue the required statement regarding deposit is in the specification. However, such a statement, found in the specification on pg 21, line 22, is not adequate. The specification does not state pMP37 or pMP42 were deposited at the ATCC. The specification does not state the name and address of the depository as required. Please read the requirements for deposit provided in the office action of 5-4-01 carefully and comply.

***Claim Rejections - 35 USC § 112***

4. Claims 1, 6, 8-10, 14-19 and 36-38 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for reasons of record.

Claim 1 as newly amended recites the limitation of an RSV protein or fragment thereof that induces production of antibodies that specifically react with the RSV protein, said protein

fragment being a truncated RSV F or G protein lacking the transmembrane anchor and cytoplasmic tail. The specification does not provide written description for any fragments of the F or G proteins of RSV that induce production of antibodies as claimed. As such, the specification does not provide written description for such fragments that are truncated RSV F or G proteins lacking the transmembrane anchor and cytoplasmic tail. Nor were such fragments known in the art at the time of filing as there was a lack of teaching regarding fragments of F or G proteins of RSV that induced antibodies. Without such guidance, it would have required one of skill in the art at the time the invention was made undue experimentation to determine any fragment of the F or G proteins of RSV that induced antibodies as claimed.

Applicants argue there is clear written description for the fragments as newly amended. Applicants argument is not persuasive. Applicants do not point to such description in the specification as originally filed. The specification does not indicate the truncated RSV F or G protein lacking the transmembrane anchor and cytoplasmic tail induces production of antibodies.

5. Claims 1, 6, 8-10, 14-19 and 36-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Support for the limitations added to claim 1 cannot be found in the specification as originally filed. The specification does not teach a truncated RSV F or G protein that lacks the transmembrane anchor and cytoplasmic tail or that induces production of antibodies as claimed.

The specification does not teach the second sequence is downstream of the first sequence. The specification does not teach the first, second, and third DNA sequence are under control of a single promoter. The specification does not teach the third DNA sequence is between the first DNA sequence and the promoter. The specification does not teach the third DNA sequence has a pair of splice sites that prevent aberrant mRNA splicing *in vivo*. As such, claim 1 as amended is new matter.

6. Claims 1, 6, 8-10, 14-19 and 36-38 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for immunogenic compositions, does not reasonably provide enablement for enhancing the immunoprotective ability of the paramyxovirus protein when expressed *in vivo* from the vector in a host. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for reasons of record.

Claim 1 as newly amended recites the limitation of a protein fragment that induces antibodies that specifically react with the RSV protein, said protein fragment being a truncated RSV F or G protein lacking the transmembrane anchor and cytoplasmic tail. The specification does not enable any fragments of the F or G proteins of RSV that induce production of antibodies as claimed. The specification does not teach F or G fragments lacking the transmembrane anchor and cytoplasmic tail or that such fragments induced antibodies. Nor were such fragments known in the art at the time of filing. Without such guidance, it would have required one of skill in the

art at the time the invention was made undue experimentation to determine any truncated RSV F or G proteins as claimed that induced antibodies.

Claim 1 recites the limitation of "the immunoprotective ability of the RSV protein or fragment thereof when expression occurs *in vivo*." Claim 36 is directed toward an "immunogenic composition" of the vector of claim 1. Applicants argue that the antibody response described in the specification was immunoprotective as claimed in 5/6 mice. Applicants argument is not persuasive. The specification teaches immunizing mice with pMP44 and obtaining 83% protection (pg 26, line 18). A 100% immunoprotective response is the hallmark of a vaccine which is the purpose of immunizing the mice. The specification does not teach the vector is fully "immunoprotective" as claimed. The specification does not provide an enabled use for an "immunogenic composition" that is not fully immunoprotective. The specification does not teach the antibodies are specific as claimed by analyzing the antibodies obtained or the specificity of the antibodies or by comparing the antibody's reactivity to other proteins.

In addition, claim 1 requires the third sequence provides the enhanced immunoprotective ability of the RSV proteins. Claim 1 is not limited to comparing the immunoprotective ability to SFV-RSV-RNA or any other particular vector. The specification does not teach whether pMP44 has "enhanced immunoprotective ability" as compared to vectors other than SFV-RSV-RNA or that the "third sequence" is what caused the greater protection as compared to SFV-RSV-RNA. Nor does the specification teach the pMP44 has the "third sequence." As such, the specification

does not provide adequate guidance for one of skill to enhance the immunoprotective ability of the paramyxovirus protein when expressed *in vivo* using the "third sequence" as claimed.

The specification does not teach the first, second, and third DNA sequence are under control of a single promoter. The specification does not teach the second sequence is downstream of the first sequence. The specification does not teach the third DNA sequence is between the first DNA sequence and the promoter. The specification does not teach the third DNA sequence has a pair of splice sites that prevent aberrant mRNA splicing *in vivo*. The specification does not teach how to use vectors having such structures. The art at the time of filing did not teach vectors having such structures. Without teaching how to make vectors having the structures claimed, the specification cannot enable one of skill to use such vectors.

7. Claims 1, 6, 8-10, 14-19 and 36-38 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite because it does not clearly set forth the structure or function of the three DNA sequences in the vector.

The first DNA sequence is indefinite because it is unclear how "complementary" the DNA sequence is to the RNA genome. In addition, it is unclear whether the phrase "and having the complement of complete alphavirus RNA genome replication" refers to the first DNA sequence or the RNA genome. The phrase "the complement" lacks antecedent basis. It is unclear what applicants consider "complete" alphavirus RNA genome replication regions that

permit *in vivo* replication. Replication regions that permit *in vivo* replication are not defined in the specification or in the art at the time of filing. It is unclear whether alphavirus regions required for replication *in vivo* in any species is the same. Overall, the structure or function of the first DNA sequence is not clearly set forth.

The second DNA sequence is indefinite because the species in the Markush Group of RSV proteins is not clearly set forth. It is unclear if the "fragment" is an RSV F or G fragment or any fragment that induces production of antibodies that are specific with the RSV protein. The term "and" should be used before the last species in the group (not "or").

It is unclear if "the RSV protein" in the phrase "antibodies that specifically react with the RSV protein" refers to the RSV F protein, the RSV G protein, a fragment of the RSV F protein, a fragment of the RSV G protein or to any RSV protein listed in the Markush group.

The third DNA sequence is indefinite because the phrase "said third DNA sequence enhancing the immunoprotective ability of the RSV protein" is unclear. It is unclear how the third DNA sequence can enhance the immunoprotective ability of the RSV proteins.

The phrase "the RSV protein or fragment thereof" lacks antecedent basis. In addition, the RSV protein in the second DNA sequence is already a fragment.

The phrase "the immunoprotective ability" of the RSV protein or fragment thereof (line 12) lacks antecedent basis.

The phrase "the promoter sequence" lacks antecedent basis.

The phrase "and comprising a pair of splice sites that prevent aberrant mRNA splicing *in vivo*" is indefinite. It is unclear to what the phrase refers. As such, it is unclear if the third sequence or the vector in general comprises such splice sites. The metes and bounds of what applicants consider aberrant cannot be determined.

The entire alphavirus sequence of the "first DNA sequence" and the splice sites of the "third DNA sequence" are not under control of the same promoter as the "second DNA sequence" as claimed.

The location of the splice sites in pMP44 (Fig. 2B) cannot be determined.

Claim 6 is indefinite because it does not further limit claim 1. The second DNA sequence cannot encode both a truncated and full length RSV protein as claimed.

Claim 8 is indefinite because it is unclear if "the alphavirus" refers to the alphavirus RNA genome or the complete alphavirus RNA genome replication regions."

Claim 9 is indefinite because the first DNA sequence is limited to alphavirus while claim 9 appears to state the first DNA sequence has Semliki Forest Virus sequence and plasmid sequence. In addition, the metes and bounds of the SFV contained in plasmid pSFVI cannot be determined.

Claim 14 is indefinite because "that of" is confusing.

Claim 15 is indefinite because "the human..." CMV intron A sequence lacks antecedent basis.

Claim 16 is indefinite because "the 3' end of the first nucleotide sequence" lacks antecedent basis.

Claim 16 is indefinite because "the first nucleotide sequence" lacks antecedent basis.

Claim 16 is indefinite because the metes and bounds of what applicants consider "proper *in vivo* cleavage" as claimed cannot be determined.

Claim 36 should refer to "the" vector of claim 1; not "a" vector of claim 1.

***Claim Rejections - 35 USC § 102***

8. Claims 1, 6, 8-10, 14-16, 18, 36 and 37 remain rejected under 35 U.S.C. 102(e) as being anticipated by Parrington (Parrington, US Patent 6,060,308, May 9, 2000) for reasons of record.

Parrington taught an SFV vector expressing the F protein of RSV. The SFV portion of the vector is the "first DNA sequence" claimed. The nucleic acid sequence encoding the F protein of RSV is the "second DNA sequence" claimed. The "second DNA sequence is downstream of the "first DNA sequence" (see Fig. 1C). The DNA just before the "second DNA sequence" is the "third DNA sequence" because the sequence can be spliced at any two sites. The promoter is the SP6 promoter (see Fig. 1C). The "third DNA sequence" is located between the promoter and "first DNA sequence." The three sequences are under the control of the SP6 promoter. The CMV immediate early promoter and rabbit β-globin intron II were used (column 4, line 11). The phrase "that enhances the immunoprotective ability..." does not bear patentable

weight because it is an intended use and does not have to occur and because it is indefinite (see 112/2nd below).

Applicants argue that Parrington does not teach a vector encoding the CMVIE promoter or rabbit β-globin intron II. Applicants argument is not persuasive because Parrington describes using these elements as a part of the vector. Therefore, Parrington taught SFV vectors encoding the F or G proteins of RSV comprising the CMVIE promoter and rabbit β-globin intron II.

***Claim Rejections - 35 USC § 103***

9. Claims 1, 6, 8-10, 14-16, 18, 36 and 37 remain rejected under 35 U.S.C. 103 as being anticipated by Dubensky (Dubensky et al., US Patent 5,814,482, Sept. 29, 1998) in view of Li (Li et al., WO 96/40945, Dec. 19, 1996) for reasons of record.

Dubensky taught an alphaviral vector encoding RSV proteins (claim 10 of '482). The alphaviral vector sequence is the "first DNA sequence" and the DNA encoding the RSV protein is the "second DNA sequence" and third DNA sequence" as claimed. The alphavirus of Dubensky is Semliki forest virus (column 11, line 67) which is equivalent to the sequence contained in plasmid pSFVI (claim 9).

The limitation of a third sequence operatively linked to the first DNA sequence (claim 1) is equivalent to the DNA encoding the RSV proteins because the phrase "that enhances the immunoprotective ability..." is indefinite (see 112/2nd above) and is an intended use which does

not have to occur. As such the phrase "that enhances the immunoprotective ability..." is not given patentable weight in considering art.

The limitation of the third DNA that comprises a pair of splice sites that prevent aberrant splicing is equivalent to the DNA sequence adjacent to the alphavirus sequence and the DNA sequence between the alphavirus sequence and the promoter taught by Dubensky. Such a sequence comprises a "pair of splice sites" because the sequence can be spliced at any two sites. In addition, the phrases "to enhance the immunoprotective ability..." and "that prevent[s] aberrant mRNA splicing *in vivo*" are intended uses and do not bear patentable weight in considering the art.

Dubensky does not teach the nucleic acid sequence of the RSV F or G proteins.

However, at the time of filing, Li taught a vector encoding the RSV F and G proteins under the control of the CMV immediate early promoter and comprising the rabbit β-globin intron II (page 14, lines 5-21).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the expression vector encoding RSV proteins taught by Dubensky to deliver the F or G protein taught by Li. Motivation is provided by Li by stating the F or G protein induce an immune response in a host (page 15, line 17). It would have been obvious to one of ordinary skill in the art at the time the invention was made to make an alphaviral vector encoding an RSV protein as taught by Dubensky wherein the F or G protein of RSV are used with the rabbit β-globin intron II sequence between the alphavirus sequence and the CMVIE

promoter as suggested by Li (page 14, line 10). It would have been obvious to one of ordinary skill in the art at the time the invention was made to place the HDV ribozyme on the 3' end of the alphavirus sequence to insure deletion of the polyA termination sequence as suggested by Dubensky (column 71, line 17) who also place the HDV ribozyme on the 3' end of the alphavirus sequence.

Applicants argue the phrases "to enhance", "that prevent" or "that enhances" bear patentable weight because they describe the function of the DNA sequence. Applicants argument is not persuasive. The mere description of a DNA sequence as a sequence "that enhances the immunoprotective ability of the RSV protein" does not describe the structure of the sequence. The description of the sequence does not adequately describe the function of the sequence because the protein may not be immunoprotective and the vector may not be introduced into a host. As such the descriptions do not adequately describe the structure or function of the sequence.

***Double Patenting***

10. Claims 1, 6, 8-10, 14-16, 18, 36 and 37 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3, 5, 6, 8 and 18-21 of U.S. Patent No. 6,060,308. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims encompass vectors lacking a Sei restriction site and the pMP37 vector claimed in 6,060,308. The pMP37 vector is disclosed

in the instant application on page 22, line 10 and in Fig. 1B, top left which according to U.S. Patent 6,060,308 lacks a SpeI restriction site (claims 1 and 8). Therefore, any of the vectors claimed in the instant invention could be linearized by SpeI restriction and lack a Spe I restriction site which is taught on page 24, line 24 as are the vectors claimed in '308. Therefore, the vectors of claims 1-3, 5, 6, 8 and 18-21 of US Patent 6,060,308 are vectors as claimed in the instant invention.

Applicants argue the claims are patentably distinct for reasons cited above regarding the 102 using Parrington (US Patent 6,060,308). Applicants arguments are not persuasive for reasons cited above in the discussion of Parrington under 102.

***Conclusion***

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-0120.

Questions of formal matters can be directed to the patent analyst, Dianiece Jacobs, who can normally be reached on Monday through Friday from 9:00 am to 5:30 pm at (703) 305-3388.

Questions of a general nature relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

If attempts to reach the examiner, patent analyst or Group receptionist are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

The official fax number for this Group is (703) 308-4242.

Michael C. Wilson

MICHAEL C. WILSON
PATENT EXAMINER